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Drug use evaluation using WHO core drug use indicators in selected general hospitals in Tigray region, Ethiopia

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Drug use evaluation using WHO core drug use indicators in selected general hospitals in Tigray region, Ethiopia

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Abstract

Objective: This study aimed to assess drug use using the World Health Organization (WHO) drug use indicators in selected general hospitals in Tigray region, Ethiopia.

Materials and Methods: A cross-sectional study was conducted from March 1, 2019, to August 30, 2019, at both Mekelle and Quiha public general hospitals. A total of 1,200 randomly selected prescription papers were assessed using WHO prescribing indicators. In addition, 200 patients who visited both outpatient clinics and hospital pharmacies were interviewed and the prescriptions were evaluated using WHO patient care indicators. Moreover, the hospitals were evaluated according to WHO facility indicators. The collected data was entered into epi-info version 7 and analyzed using SPSS for Windows, version 21.

Result: The average number of medicines per prescription was 1.69 (± 0.81). Prescriptions with antibiotics and injectable were 58.15 % and 15.9 % respectively. The percentage of medicines prescribed with a generic name and those from the essential medicines list of Ethiopia were 974 (97.5%) and 970 (88.1%) in Mekelle and Quiha hospital respectively. In terms of patient care, average consultation and dispensing times were 6.56 (± 3.48) minutes and 22.79 (± 21.7) seconds

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3 respectively. The proportion of drugs actually dispensed, those correctly labeled as well as the
4 proportion of patients knowing their dosing regimen were 81.2%, 32.7%, and 56.9% respectively.
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8 Only 77.5% of key drugs were available in stock during the study period.
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10 **Conclusion:** In our study both prescribing and patient care indicators showed significant deviation
11 from the World Health Organization's optimal levels indicating the presence of inappropriate
12 medicine use in the hospitals. Strategies to improve both prescribing and dispensing practice
13 should be implemented for promoting rational use of medicines.
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20 Keywords: Drug use evaluation, Prescribing Indicator, Patient Care Indicators, Facility Indicators
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23 **Strengths and limitations of this study**

- 24 • As strengths, the study used all the three WHO core drug use indicators to evaluate the
25 drug use.
 - 26 • The study included a good number of prescriptions and patients for drug use evaluation.
 - 27 • The study provides alarming information for hospitals and all relevant stakeholders on
28 the use of antibiotics which represents a very high percentage per prescription.
 - 29 • The study does not examine the cause of irrational drug use and did not confirm that drug
30 use was consistent with the diagnosis.
 - 31 • The study period was short.
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45 **Introduction**

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47 The rational use of drugs depends on rational prescribing, correct dispensing and adherence to
48 treatment by patients (1). According to the World Health Organization (WHO), a medicine is used
49 rationally if patients received the appropriate medicines, in doses that meet their individual
50 requirements, for an adequate period of time and with an affordable cost (2). The concept of
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3 rational drug use can be summarized as the right medicine at the right dose by the right route at
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5 the right time for the right patient ('five rights') (3).
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8 On the contrary, irrational, inappropriate, improper, or incorrect use of medicines is termed to have
9
10 occurred when one or more of the above-mentioned conditions are not met (2). Irrational use of
11
12 medicines is a global challenge, especially in developing countries. Different factors are attributed
13
14 to the irrational use of medicines including patients, prescribers, workplace, supply system which
15
16 encompasses industry influences, regulation, drug information and misinformation, and
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18 combination of these factors (4). Irrational prescribing is a major problem encountered and it is
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20 due to lack of knowledge about medicines, unethical medicine promotions and bad prescribing
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22 habits of clinicians (5, 6).
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27 Medicine utilization studies are important tools to evaluate whether medicines are properly utilized
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29 in terms of efficacy, safety, convenience and economic aspects at all levels in the chain of medicine
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31 use (7). In order to improve medicine use practices, objective method of assessments at health
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33 facilities is very important as it helps to improve use patterns and prescribing behaviors. WHO
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35 core drug use indicators are developed intended for this purpose by the WHO Action Program on
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37 Essential Drugs and International Network for Rational Use of Drugs (INRUD). These indicators
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39 are highly standardized that do not need national adaptation and are recommended to be included
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41 in any medicine use evaluation (8).
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46 Prescribing indicators include average number of medicines prescribed per encounter, percentage
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48 of those prescribed by generic name and those from national essential medicines list (EML),
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50 percentage of encounters with antibiotics and those with injections prescribed. Patient care
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52 indicators, on the other hand, include average consultation and dispensing times, percentage of
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54 medicines actually dispensed and of those adequately labeled, as well as patients' knowledge of
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3 correct dosage. Facility indicators assess the availability of copy of EML and those of key
4
5 medicines available in the health facility (9).
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8 Ethiopia has a national drug policy introduced in 1993 which aims to meet the demand for essential
9
10 medicines together with appropriate use, making them affordable to the public as well as ensuring
11
12 their safety, efficacy, and quality. The policy also encourages domestic manufacturing, enhancing
13
14 manpower training and research and development of medicines as well as devising ways to
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16 integrate traditional medicines into conventional medicine as objectives (10). Despite these
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18 objectives' studies conducted so far reported gaps in rational medicine use with a high percentage
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20 of encounters with antibiotics and injections prescribed (11, 12).
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25 Considering the very large population size of Ethiopia and the diversity of geographic areas, there
26
27 are very few studies on medicine use conducted so far. Therefore, this study was carried out to
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29 evaluate drug use and contribute in narrowing of the information gap in the documentation of drug
30
31 use patterns in Ethiopia using WHO's core drug use indicators.
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34 **Methods and Materials**

35 **Study setting and period**

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38 The study was conducted at Mekelle and Quiha general hospitals between March 1, 2019 and
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40 August 30, 2019. Both hospitals are located in Mekelle which is 783km from the capital city of
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42 Ethiopia.
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47 **Study design and population**

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50 A cross sectional study was employed. The target population of this study were all patients who
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52 were visiting outpatient department of Mekelle and Quiha hospital during the study period.
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3 Those patients 18 years and above with a prescription recorded from 2017 to 2019 were
4 included. Patients who were not willing to participate were excluded from the study.
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8 **Sampling technique and procedure**

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10 World Health Organization recommends assessments of at least 600 prescriptions and 100 patients
11 per each hospital for assessment of prescribing, and, patient care indicators respectively.
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13 Accordingly, we had included 600 randomly selected sample prescriptions among those recorded
14 from 1 January 2017-1 June 2019. Twenty key drugs were selected from each hospital as per WHO
15 recommendation which is a minimum of 15 essential drugs in each health facility (9).
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23 **Data collection instruments and process**

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26 Three well-trained pharmacy personnel were recruited and deployed in each hospital. One of them
27 was collecting prescribing indicators by using prescriptions and prescription registration books,
28 while the others were collecting the patient care indicators and the facility indicators. Specific
29 types of data necessary to measure the prescribing indicators were recorded for each prescription
30 and entered to the prescribing indicator form.
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38 Data on medicine use pattern was collected by using WHO's prescribing and patient care
39 indicators. In measuring the former, the average number of medicines prescribed per encounter,
40 the percentage of medicines prescribed with generic names and those prescribed from EML, the
41 percentage of prescription encounters which ended up with antibiotics and those with injections
42 prescribed were collected. In collecting data on these indicators, immunizations of children were
43 not considered as injections. In measuring the proportion of medicines prescribed with generic
44 names, the EML of Ethiopia was used as the main source of generic names (13).
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3 For patient care indicators measurement, data on average consultation and dispensing times,
4 percentages of medicines actually dispensed and of those adequately labeled as well as patients'
5 knowledge of dosage schedule of medicines were collected. In this part of the study patients aged
6 18 or older were included. Consultation time and dispensing time was obtained by recording the
7 time that the patient spent with his physician and pharmacist respectively
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15 In determining patients' knowledge of their dosage regimen, patients were asked to explain what
16 they know about the medicine dispensed for them.
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19 Facility indicators were availability of formulary, essential drugs, standard treatment guidelines,
20 and key drugs observed at the time of the visit.
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24 **Operational definitions**

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27 Drug use evaluation is a systematic approach that assesses the appropriateness, safety, and
28 effectiveness of a medications to improve patient care.
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31 **Percentage of drugs prescribed by generic name:** It measures the tendency to prescribe by
32 generic name.
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36 **Percentage of drugs prescribed from list of essential drugs:** It measures the degree to which
37 practices conform to a national drug policy.
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41 **Average number of drugs per encounter:** Average number of drugs per encounter measures the
42 degree of poly pharmacy.
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45 **Average consultation time:** The average time that physicians spends with patients. It doesn't
46 include waiting time.
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50 **Average dispensing time:** The average time that the pharmacists spend with patients while
51 actually dispensing the medications.
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Data analysis procedure

The data collected were entered to, cleaned and analyzed using Statistical Packages for Social Sciences (SPSS) version 20. The data on prescribing indicators as well as patient care indicators were described using frequency, percentage, mean and standard deviation (SD).

Patient and Public Involvement

Patients and/or the public were not directly involved in this study.

Results

Prescribing indicators

Six hundred prescriptions from each hospital were assessed. On average, 1.69 (± 0.81) drugs were prescribed and 49.7% of the prescriptions contain one drug followed by two drugs (35%) (Table1).

Table 1: Number of drugs per prescribing encounters (degree of polypharmacy) in Mekelle and Quiha hospital March1, 2019 – August 30, 2019 (n=1200)

Number of drugs	QH	MH	Overall result	WHO
One	306(51)	286(47.7)	592(49.7)	
Two	206 (34.3)	214(35.7)	420(35)	
Three	72 (12)	82(13.7)	154(12.85)	
Four	15 (2.5)	17(2.8)	32(23.5)	
Five	1(0.2)	1(0.2)	2(0.2)	
Average	1.67 ((± 0.8))	1.72((± 0.82))	1.69((± 0.81))	≤ 2 (1.6–1.8)

QH: Quiha hospital, MH: Mekelle hospital

From the total of the prescriptions, 2028 drugs were prescribed of which 1944(92.8%) of the drugs were prescribed in generic name. More than fifty percent (58.15%) of the prescriptions contain antibiotics while 191 (15.9%) include at least one injectable medication (Table 2).

Table 2: Percentages of encounters with generic prescription, antibiotics, and injections

Prescribing indicators		QH	MH	Overall result	WHO standard
Percentage of drugs with generic prescription	Number of drugs prescribed	999	1029	2028	
	Number of drugs prescribed by generic name	974	970	1944	
	Number of drugs prescribed by generic name	97.5	88.1	92.8	
Percentage of encounters with antibiotics	Total number of Encounters with antibiotic	392	306	698	
	% of encounters with antibiotics	65.3	51	58.15	< 30 (20–26.8%)
Percentage of encounters with injections	Encounters with injections	56	135	191	
	% of encounters with injections	9.3	22.5	15.9	(13.4–21.1%)
Percentage of drugs on essential drug list		974	930	94%	100%

QH: Quiha hospital, MH: Mekelle hospital

Amongst antibiotics prescribed, 279 of them were amoxicillin or Amoxicillin / Clavulanic acid followed by Ceftriaxone (100) (Table 3).

Table 3: Antibiotics prescribed in Mekelle and Quiha hospital

Antibiotics	Frequency		Overall
	QH	MH	
Acyclovir	2	-	2
Albendazole	16	7	23
Amoxicillin	160	76	236
Ampicilin	1	9	10
Amoxicillin /Clavulanic acid	15	28	43
Azitromycin	19	16	35
sulfamethoxazole/trimethoprim	13	11	24
Ceftriaxone	33	57	90
Cephalexin	20	35	55
Ciproflocin	56	44	100
Clarithromycin	8	1	9
Clotrimazole vaginal supp.	3	-	3
Cloxacillin	21	11	32
Coarthem	2	-	2
Doxycycline	13	7	20
Acetazolamide	3	-	3
Erythromycin	2	2	4
Fluconazole	1	-	1
Gentamycin	1	2	3
Ketoconazole	4	-	4
Mebendazole	11	5	16
Metronidazole	42	40	82
Norfloxacin	17	11	28
Praziquantal	1	-	1
Crystalline Penicillin	-	1	1
Ceftazidime	-	2	2
Tinidazole	14	17	31
Pantoprazole	1	-	

Patient care indicators

On average each person spends around 7 minutes with the physician while only 22 seconds with pharmacist. 81.2% of the prescribed drugs were actually dispensed of which 32.7% of them adequately labeled and 56.9% of the patients knows about the correct dosage of their medications (Table 4).

Table 4: Percentage and average descriptions of patient care indicators

Patient care indicators	QH	MH	Overall	WHO standard
Average consultation time (minute)	3.66±2.19	9.46±4.77	6.56±3.48	10 min
Average dispensing time (Sec)	21.53±19.89	24.04±23.5	22.79±21.7	>180 s
Total number of drugs prescribed	189	171	360	
Total number of drugs dispensed	170	124	294	
Percentage of drugs actually dispensed	89.9	72.5	81.2	100%
# of drugs adequately labelled	29	50	79	
Percentage of drugs adequately labelled	15.4	50	32.7	
Knows dosage	25(25%)	48 (88.8%)	56.9	

QH: Quiha hospital, MH: Mekelle hospital

Health facility indicators

Both Mekelle and Quiha hospital have their own formulary, essential drug list and standard treatment guideline. From the list of key drugs of the hospitals on average 77.5% of them were available in stock (Table 5).

Table 5: Availability of the key drugs in the hospitals

List of key drugs	Availability in QH	Availability in MH
Amoxicillin/clavulanic acid	✓	X
Ciprofloxacin tablet	✓	✓
Cloxacillin capsule	✓	✓
Azitromycin	✓	X
Diclofenac injection	✓	✓
Diclofenac tablet	✓	✓
Tramadole	X	✓
Metronidazole	✓	✓
NPH	✓	✓
Nefidipine	X	✓
Laxis	X	✓
Spironolactone	X	✓
Ceftriaxone	✓	X
Vancomycin	✓	✓
Metformin	✓	✓
Enalapri	✓	✓
Cephalexin	✓	✓
Ferrous sulfata	✓	✓
Paracetamol syrup	✓	X
Amilodipine	✓	X

QH: Quiha hospital, MH: Mekelle hospital

Discussion

In the present study among the prescribing indicators, the average number of medicines per prescription was found to be within the WHO's acceptable range of 1.6 to 1.8 (14). This figure has showed a good trend in preventing risks associated to polypharmacy. The finding was also comparable with studies done in different parts of Ethiopia including Jimma (1.59) (15), Hawassa University Teaching Referral (1.9) (11) and Bahir Dar hospital (1.8) (12). However, compared to findings from other studies in Ethiopia including Debre Tabor Hospital (2.2) (11), Hiwot Fana specialized University (2.49) (16) and Karamara general hospital (2.46)(17) as well as those done abroad like in Iran (3.03)(18), South Africa (3.2)(19) and India (2.9) (20); the figure in the present study recorded lower average number of medicines per prescription.

In terms of percentage of medicines prescribed by generic name, the result of the present study (92.8%) is lower compared to WHO's standard (100%) and it is in line with study done at Hawassa University Hospital (98.7%) (11), Hiwot Fana specialized University hospital (97.4 %) (16) as well as a finding in selected health centres of eastern Ethiopia (97 %) (21). This indicates that there is a gap in ensuring patients to get cost-effective medicines on the side of prescribers and the health institution. So this cost ineffective prescribing practice will promote noncompliance. However, it is higher compared to findings of , India (13.34%)(20), South Africa (45.2%) (19), Nepal (13%) (22) and Nigeria (49.5%) (23).

The percentage of encounters with antibiotics prescribed, which is 58.15 % in the present study, is higher compared to the WHO's standard recommendation of 20 to 26.8% per prescription (8), but it is comparable with study conducted in public hospitals in Eastern Ethiopia (57.87) (17) and Hawassa teaching referral hospital (58.1) (11). However, it showed lower figure compared to a study conducted in selected health centres in Eastern Ethiopia (85.5) (24). This huge variation can

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3 be explained due to the high prevalence of infectious disease in developing countries that may led
4 to prescribing of antibiotics, however high antibiotic prescribing could lead to antimicrobial
5 resistance which is an eminent threat of global health (25).
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10 The percentage of encounters with injection prescribed in this study was within WHO standard
11 range, from 13.4% to 21.1%. This good practice will prevent patients from injection site related
12 infections and injection site pain. However, there is a gap in prescribing according to essential
13 medicine list of Ethiopia compared to the WHO standard of a 100% (8) and to that of the national
14 assessment results of 2003 (99%) (26), but it was similar to the finding reported in Hawassa
15 (96.6%) (11).
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25 In this study the average consultation time that the prescribers spent with patients was
26 approximately 7 minutes and this is comparable with findings conducted in Saudi Arabia (7.3
27 minutes) (27). However, it is higher in comparison with studies conducted in public hospital (4.6
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57 minutes) (27). However, it is higher in comparison with studies conducted in public hospital (4.6
58 minutes) (27). However, it is higher in comparison with studies conducted in public hospital (4.6
59 minutes) (27). However, it is higher in comparison with studies conducted in public hospital (4.6
60 minutes) (27). However, it is higher in comparison with studies conducted in public hospital (4.6

39 The average dispensing time recorded in the present study was approximately 23 seconds. This is
40 very low compared to the standard WHO recommendation which is 18 minutes (14), study
41 conducted in public hospital (276.5) (28) and health centres (162) (28) in eastern Ethiopia. The
42 lower the dispensing time the poorer would be the understanding of the patients about their
43 medication which this may lead to frequent encounter of drug therapy problems.
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51 The percentage of drugs actually dispensed out of the total drugs prescribed to the patients stood
52 at 80 % compared to the recommended 100% (6). This was due to lower than availability of
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3 medicines as the result of frequent stock out of medicines. This is also associated to availability
4 issues at national level as well as to medicine supply system problems.
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8 Regarding the adequacy of labeling of medicines dispensed, only slightly over one-third of
9 medicines were appropriately labeled which is far to the recommended level 100% (8). High
10 patient load encountered at outpatient pharmacy department and negligence of the pharmacists
11 together with low concern for the issue from the hospital side could be implicated to the very low
12 level of performance in this indicator.
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20 In this study only about half of the patients knew the dosage schedules of their medicines
21 prescribed to them which is far below the desired 100%. The low level of awareness of patients
22 could be attributed to the short dispensing time which hinders appropriate transfer of advice by
23 pharmacy professionals to patients as well as the rare practice of adequate labeling of medicines.
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30 Both of the hospitals involved in the current study have their own essential drug list and standard
31 treatment guideline. Only 7.5% of key drugs were in stock and this is low with 100 % WHO
32 recommendation. Absence of key drugs may impair patient care and compromise patient quality
33 of life.
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40 Finally, our study is not without limits. The study only used two centers and it was better to use
41 more centers. The study also does not examine the cause of irrational drug use or confirm that the
42 drug use was consistent with the diagnosis. It was also better if the study was conducted over a
43 longer period.
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49 **Conclusion**

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51 On the basis of the current findings, the prescribing practices for antibiotic use, prescribing from
52 EDL and injection use showed a great deviation from the standards recommended by WHO. Over
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3 use of antibiotics facilitate the emergence of antimicrobial resistance which is a major challenge
4 for our globe. Generic prescribing showed little deviation from the standard whereas the average
5 number of drugs per encounter lay within the range of WHO. Relatively low generic prescribing
6 compared with WHO standard coupled with shorter consultation and dispensing time may lead to
7 frequent encounters of drug therapy problems. Therefore, having this as a baseline data
8 interventional strategy should be designed to reverse the existing problems (managerial,
9 educational and regulatory) and modernize the drug utilization patterns on public hospitals.

19 **Abbreviation and acronyms**

21 DUE: Drug use evaluation, EDL: Essential drug list, WHO: World health organization, HFSUH:
22 Hiwot Fana Specialized Hospital, QH: Quiha Hospital, MH: Mekelle Hospital, INRUD:
23 International Networks for Rational use of medicines.

28 **Ethical Considerations**

30 The study was approved by the institutional review board of Mekelle University (reference
31 number: ERC/224/2019). Based on this a letter of support was written from Tigray regional health
32 bureau. During data collection on patient care indicators, a written consent was obtained from each
33 participant after provision of all the necessary information. In addition, the data collected in the
34 study did not use patient identifiers and were kept strictly confidential and were used only for the
35 purpose of the study.

45 **Acknowledgments**

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48 sincere cooperation and support.

Competing interests

The authors declare that they have no competing interests. The funder of this study has no any involvement in this study.

Availability of data and materials

The data of this study are available from the corresponding author on reasonable request.

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Patient consent for publication

Not required

Author's contribution

SG and AK designed the study, supervising data collection, conducted data analysis, wrote the first draft of the manuscript. SG, KG, AK and HN provide critical comments, revised and finalized the manuscript. All authors read and approved the final manuscript.

Reference

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4 and 5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 and 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5 and 6
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	--
		(d) If applicable, describe analytical methods taking account of sampling strategy	--
		(e) Describe any sensitivity analyses	--
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	--
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	---
Outcome data	15*	Report numbers of outcome events or summary measures	7-11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	---
		(b) Report category boundaries when continuous variables were categorized	---
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	----
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	---
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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3 Drug use evaluation using WHO core drug use indicators in selected general hospitals in
4 Tigray region, Ethiopia
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16 Abstract

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19 **Objective:** This study was aimed to assess drug use using the World Health Organization
20 (WHO) drug use indicators in selected general hospitals in Tigray region, Ethiopia.
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23 **Materials and Methods:** A total of 1200 randomly selected prescriptions from Mekelle and
24 Quiha hospital that were recorded from 1 January 2017 to 1 June 2019 were cross-sectionally
25 assessed from 1 March 2019 to 30 August 2019 using WHO prescribing indicators. Further,
26 100 patients from each hospital who visited both outpatient clinics and hospital pharmacies
27 were interviewed, and prescriptions evaluated in according to WHO patient care indicators.
28 Moreover, the hospitals were evaluated according to WHO facility indicators.
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33 **Result:** The average number of medicines per prescription was 1.69 (± 0.81). Prescriptions
34 containing antibiotics and injectable were 58.2% and 15.9% respectively. The percentage of
35 medicines prescribed with a generic name and from essential medicines list of Ethiopia were
36 974 (97.5%) and 970 (88.1%) in Mekelle and Quiha hospital, respectively. The patients spent
37 an average of 6.56 (± 3.48) minutes with their General Practitioner, whilst only 22.79 (± 21.7)
38 seconds with their pharmacist. Of the patients interviewed, 56.9% knew their dosing regimen
39 and only 32.7% of them were correctly labelled.
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47 **Conclusion:** The finding of this study revealed significant deviation from WHO optimal levels
48 suggesting the need for improvement in medicine utilization in those hospitals. Understanding
49 the factors that contributed for such gaps and implementing correct measures is required to
50 conform with the recommended WHO standard of care.
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54 **Keywords:** Drug use evaluation, Prescribing Indicator, Patient Care Indicator, Facility
55 Indicator
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Strengths and limitations of study

- The study utilized all WHO core drug use indicators to assess quality of patient care in hospital setting.
- An important evidence about rational drug use is provided in an area rarely assessed.
- The study did not try to identify the factors that contributed for the observed deviation making it difficult to propose improvement strategies.
- As diagnosis was missing in considerable number of prescriptions, we did not confirm that the drugs were prescribed for right diagnoses.

Introduction

The rational use of drugs depends on rational prescribing, correct dispensing and adherence to treatment by patients¹. According to the World Health Organization (WHO), a medicine is used rationally if patients received the appropriate medicines, in doses that meet their individual requirements, for an adequate period of time and with an affordable cost². The concept of rational drug use can be summarized as the right medicine at the right dose by the right route at the right time for the right patient ('five rights')³.

On the contrary, irrational use of medicines is termed to have occurred when one or more of the above-mentioned conditions are not met² and it is a global challenge with a highest prevalence in developing countries. Patients, prescribers, workplace, supply system may attribute for irrational drug use⁴ because of limited knowledge about medicines, unethical medicine promotions and improper prescribing habits of clinicians^{5 6}.

WHO drug use indicators are used to evaluate rational drug use at all levels in the chain of medicine utilization using objective assessment methods. WHO core drug use indicators, developed by WHO Action Program on Essential Drugs and International Network for Rational Use of Drugs (INRUD), are highly standardized to be used for drug use evaluations without further national validation^{7 8}.

Prescribing indicators include average number of medicines prescribed per encounter, percentage of those prescribed by generic name and those from national essential medicines list (EML), percentage of encounters with antibiotics and those with injections prescribed. Patient care indicators, on the other hand, include average consultation and dispensing times, percentage of medicines actually dispensed and of those adequately labeled, as well as patients' knowledge of correct dosage. Facility indicators assess the availability of copy of EML and

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3 those of key medicines available in the health facility⁹. Ethiopia has introduced a national drug
4 policy in 1993 with the aim of meeting the demand for essential medicines together with
5 appropriate use, making them affordable to the public as well as ensuring their safety, efficacy,
6 and quality. The policy also encourages domestic manufacturing, enhancing manpower
7 training and research and development of medicines as well as devising ways to integrate
8 traditional medicines into conventional medicine as objectives¹⁰. Despite these objectives'
9 studies conducted so far reported gaps in rational medicine use with a high percentage of
10 encounters with antibiotics and injections prescribed^{11 12}. Considering the very large population
11 size of Ethiopia and the diversity of geographic areas, there are very few studies on medicine
12 use conducted so far. Therefore, this study was carried out to evaluate drug use and contribute
13 in narrowing of the information gap in the documentation of drug use patterns in Ethiopia using
14 WHO's core drug use indicators.
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24 **Methods and Materials**

25 **Study setting and period**

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27 The study was conducted both in Mekelle and Quiha general hospitals between 1 March 2019
28 and 30 August 2019. Both hospitals are located in Mekelle, the capital city of Tigray regional
29 state, Ethiopia.
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35 **Study design and population**

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37 All prescriptions recorded from 1 January 2017 to 1 June 2019 were considered. Of which,
38 randomly selected prescriptions were retrospectively for their quality using WHO prescribing
39 indicators during the study period [1 March 2019 and 30 August 2019]. All patients who were
40 visiting outpatient department of Mekelle and Quiha hospital during the study period were also
41 used as a target population. Of note, patients aged less 18 or not willing to participant in the
42 study were excluded.
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49 **Sampling technique and procedure**

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51 World Health Organization recommends assessments of at least 600 prescriptions and 100
52 patients per each hospital for drug use evaluation. Accordingly, we had included 600 randomly
53 selected sample prescriptions recorded from 1 January 2017 to 1 June 2019 from each hospital.
54 Twenty key drugs were selected from each hospital as per WHO recommendation which is a
55 minimum of 15 essential drugs in each health facility⁹.
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Data collection instruments and process

Three well-trained pharmacy personnel were recruited and deployed in each hospital. One of them was collecting prescribing indicators by using prescriptions and prescription registration books, while the others were collecting the patient care indicators and the facility indicators. Specific types of data necessary to measure the prescribing indicators were recorded for each prescription and entered to the prescribing indicator form. Data on medicine use pattern was collected by using WHO's prescribing and patient care indicators. In assessing patient care indicators, the average number of medicines prescribed per encounter, the percentage of medicines prescribed with generic names and those prescribed from EML, the percentage of prescription encounters which ended up with antibiotics and those with injections prescribed were collected. However, immunizations of children were not considered as injections. In measuring the proportion of medicines prescribed with generic names, the EML of Ethiopia was used as the main source of generic names¹³.

For patient care indicators measurement, consultation time and dispensing time was obtained by recording the time that the patient spent with his physician and pharmacist respectively in patients aged greater than 18 years. In determining patients' knowledge of their dosage regimen, patients were asked to explain what they know about the medicine dispensed for them. Facility indicators were availability of formulary, essential drugs, standard treatment guidelines, and key drugs at the time of the visit were assessed.

Operational definitions

Drug use evaluation is a systematic approach that assesses the appropriateness, safety, and effectiveness of a medications to improve patient care.

Percentage of drugs prescribed by generic name: It measures the tendency to prescribe by generic name.

Percentage of drugs prescribed from list of essential drugs: It measures the degree to which practices conform to a national drug policy.

Average number of drugs per encounter: Average number of drugs per encounter measures the degree of poly pharmacy.

Average consultation time: The average time that physicians spends with patients. It doesn't include waiting time.

Average dispensing time: The average time that the pharmacists spend with patients while dispensing the medications.

Data Analysis Procedure

The data collected were entered and analyzed using Statistical Packages for Social Sciences (SPSS) version 20. The data on prescribing indicators as well as patient care indicators were described using frequency, percentage, mean and standard deviation (SD).

Patient and Public Involvement

Patient and/or the public were not directly involved in this study.

Results

Prescribing indicators

A total of 1200 prescriptions, 600 from each hospital were evaluated using WHO prescribing indicators. On average, 1.69 (± 0.81) drugs were prescribed and 44.7% of the prescriptions contain one or two drugs (Table 1).

Table 1: Number of drugs per prescribing encounter in the selected general hospitals

Number of drugs	Quiha hospital n (%)	Mekelle hospital n (%)	Overall result N (%)	WHO standard ¹⁴
One	306 (51)	286 (47.7)	592 (49.7)	
Two	206 (34.3)	214 (35.7)	420 (35)	
Three	72 (12)	82 (13.7)	154 (12.9)	
Four	15 (2.5)	17 (2.8)	32 (23.5)	
Five	1 (0.2)	1 (0.2)	2 (0.2)	
Average	1.67 (± 0.8)	1.72 (± 0.82)	1.69 (± 0.81)	≤ 2 (1.6-1.8)

From the total of 1200 prescriptions, 2028 drugs were prescribed of which 1944 (92.8%) were prescribed in generic name. More than fifty percent (58.2%) of the prescriptions contained antibiotics whilst 191 (15.9%) include at least one injectable medication (Table 2).

Table 2: Percentages of encounters with generic drugs, antibiotics, and injections in the selected general hospitals

Prescribing indicators		Quiha hospital	Mekelle hospital	Overall result (N)	WHO standard ¹⁴
Generic prescription	Drugs prescribed, n	999	1029	2028	
	Drugs prescribed in generic name, n (%)	974 (97.5)	970 (94.3)	1944 (95.6)	
Antibiotics	Prescriptions with antibiotics, n (%)	392 (65.3)	306 (51)	698 (58.2)	< 30% (20–26.8)
Injections	Prescriptions with injections, n (%)	56 (9.3)	135 (22.5)	191(15.9)	13.4–21.1%
Drugs from essential drug list, n (%)		974 (97.5)	930 (90.4)	1904 (93.9)	100%

Amoxicillin or Amoxicillin / Clavulanic acid, and Ceftriaxone were commonly prescribed antibiotics (Table 3).

Table 3: Antimicrobial/Antibiotics prescribed in the selected general hospitals

Class of Antimicrobial agent	Frequency, n		Overall	
	Quiha hospital	Mekelle hospital		
Amoxicillin	160	76	236	
Ciprofloxacin	56	44	100	
Ceftriaxone	33	57	90	
Metronidazole	42	40	82	
Antibacterial agents	Cephalexin	20	35	55
	Amoxicillin /Clavulanic acid	15	28	43
	Azithromycin	19	16	35
	Cloxacillin	21	11	32
	Norfloxacin	17	11	28
	Sulfamethoxazole/Trimethoprim	13	11	24
	Doxycycline	13	7	20
	Ampicillin	1	9	10
	Clarithromycin	8	1	9
	Erythromycin	2	2	4
	Gentamycin	1	2	3

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3		Ceftazidime	-	2
4				2
5		Crystalline Penicillin	-	1
6				1
7	Antiprotozoal/anthelmintics	Tinidazole	14	17
8				31
9		Albendazole	16	7
10				23
11		Mebendazole	11	5
12				17
13		Coarthem	2	-
14				2
15		Praziquantel	1	-
16	Antifungal			1
17		Ketoconazole	4	-
18				4
19		Clotrimazole vaginal supp	3	-
20				3
21		Fluconazole	1	-
22	Antiviral			1
23		Acyclovir	2	-
24				2
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Patient care indicators

On average each patient spent approximately 7 minutes with his/her General practitioner, whilst only 22 seconds with his/her pharmacist. 81.2% of the prescribed drugs were dispensed. Of which, 32.7% of them were adequately labelled. 56.9% of the patients knew about their dosage regimen of their medications (Table 4).

Table 4: Assessment of patient care using WHO patient care indicators in selected general hospitals

Patient care indicators	Quiha hospital	Mekelle hospital	Overall	WHO standard
Average consultation time (Minute)	3.66±2.19	9.46±4.77	6.56±3.48	10 min
Average dispensing time (Sec)	21.53±19.89	24.04±23.5	22.79±21.7	>180 seconds
Total number of drugs prescribed	189	171	360	
Total number of drugs dispensed	170	124	294	
Percentage of drugs actually dispensed	89.9	72.5	81.2	100%
Number of drugs adequately labelled	29	50	79	
Percentage of drugs adequately labelled	15.4	50	32.7	
Knows dosage	25(25%)	48 (88.8%)	56.9	

Health facility indicators

Both Quiha and Mekelle hospitals have their own formulary, essential drug list and standard treatment guideline. From the list of key drugs of the hospitals on average 77.5% of them were available in stock (Table 5).

Table 5: Availability of key drugs in selected general hospitals

List of key drugs	Quiha hospital	Mekelle hospital
Amoxicillin/clavulanic acid	✓	X
Ciprofloxacin tablet	✓	X
Cloxacillin capsule	✓	X
Azithromycin	✓	X
Diclofenac injection	✓	✓
Diclofenac tablet	✓	✓
Tramadol	X	✓
Metronidazole	✓	✓
Insulin	✓	✓
Nifedipine	X	✓
Lasix	X	✓
Spironolactone	X	✓
Ceftriaxone	✓	X
Vancomycin	✓	✓
Metformin	✓	✓
Enalapril	✓	✓
Cephalexin	✓	✓
Ferrous sulphate	✓	✓
Paracetamol syrup	✓	X
Amlodipine	✓	X

Discussion

In this study, we have revealed within the WHO acceptable standard for average number of drugs per prescription. The finding was comparable with studies done in different parts of Ethiopia including Jimma (1.59)¹⁵, Hawassa University Teaching Referral (1.9)¹¹ and Bahir Dar hospital (1.8)¹². However, studies in Debre Tabor (2.2)¹², Felege Hiwot referral hospital (2.49)¹⁶ and Karamara public general hospital in Ethiopia (2.46)¹⁷ reported higher average number of drugs per prescription. Such discrepancy may be attributable to difference in the level of awareness among clinicians working in different part of the country.

In terms of percentage of medicines prescribed by generic name, the result of the present study (92.8%) is lower compared to WHO's recommended standard value (100%). Similar results were reported at Hawassa University Hospital (98.7%)¹¹, Felege Hiwot specialized University hospital (97.4 %)¹⁶ and selected health centres in Eastern Ethiopia (97 %)¹⁸. This could be due to increasing promotion of brand drugs influencing clinicians to prescribe brand names. This suggests that there is a gap in ensuring patients to get cost-effective medicines on the side of prescribers and the health institution, which in turn reduce health seeking behaviour of the community¹⁹.

The percentage of encounters with antibiotics, which is 58.2% in the present study, is higher compared to the WHO's standard recommendation of 20 to 26.8% per prescription (8), but it is comparable with study conducted in public hospitals in Eastern Ethiopia (57.9%)¹⁷, and Hawassa teaching referral hospital (58.1%)¹¹. However, it lower compared to a study conducted in selected health centres in Eastern Ethiopia (85.5%)¹⁸. High prevalence of infectious disease in developing countries may account for such higher antibiotic prescribing than the recommended level by WHO. However, such problematic level of antibiotic prescribing may lead to antimicrobial resistance which is an eminent threat of global health²⁰. The percentage of encounters with injection prescribed in this study was within WHO standard range.

A deficiency was noted in terms of prescribing according to essential medicine list of Ethiopia compared to the WHO standard of a 100% (8) and to that of the national assessment results of 2003 (99%)²¹. This may attributable to clinical condition of the patients, patient preference, clinician decision and availability of the medications.

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3 In this study the average consultation time that the patients spent with clinicians was
4 approximately 7 minutes which is higher in comparison with studies conducted in public
5 hospital (4.6 minutes)¹⁷. The duration, however, doesn't seem to be sufficient for to make
6 physical examination and select the best available treatment choices. High patient load could
7 have contributed for such below the optimal duration of consultation time. The average
8 dispensing time recorded in the present study was approximately 23 seconds. This is
9 significantly lower than standard WHO recommendation which is 180 seconds⁸. The lower the
10 dispensing time the poorer would be the understanding of the patients about their medication
11 which this may lead to frequent encounter of drug therapy problems. The percentage of drugs
12 actually dispensed out of the total drugs prescribed to the patients stood at 80 % compared to
13 the recommended 100%⁶. Frequent stock out of medicines may account for such finding.
14 Regarding the adequacy of labelling of medicines dispensed, only slightly over one-third of
15 medicines were appropriately labeled which is far from the recommended level, 100%⁸. High
16 patient load encountered at outpatient pharmacy department and negligence of the pharmacists
17 together with poor concern and follow up from the hospital side could be implicated for such
18 low level of performance in this indicator. Of note, only about half of the patients knew the
19 dosage schedules of their medicines prescribed to them, which is far below the expected level,
20 100%.

21
22 Both Quiha and Mekelle hospital have their own essential drug list and standard treatment
23 guideline. Only 7.5% of key drugs were in stock and this is low with 100 % WHO
24 recommendation. Absence of key drugs may impair patient care and compromise patient
25 quality of life.

26
27 The study has several strengths. Firstly, it utilized all WHO core drug use indicators to assess
28 quality of patient care in hospital setting. Secondly, we included WHO recommended sample
29 size. Finally, it provided an important evidence about rational drug use in a study area which
30 is rarely assessed. The study has also limitations. The study did not try to identify the factors
31 that contributed for the observed deviation making it difficult to propose improvement
32 strategies. However, it can be utilized as a benchmark for further studies. As diagnosis was
33 missing in considerable number of prescriptions, we did not confirm that prescribed drugs were
34 consistent with the diagnoses.

Conclusion

The findings of the present study showed prescribing practices for antibiotic use, prescribing from essential drug list and injection use were not within acceptable WHO recommendations. Overuse of antibiotics facilitate the emergence of antimicrobial resistance which is a major challenge for our globe. Generic prescribing showed little deviation from the standard whereas the average number of drugs per encounter lay within the range of WHO. Poor generic prescribing coupled with shorter consultation and dispensing time may lead to frequent encounters of drug therapy problems. Future studies should look for factors attributable for the observed gaps to improve patient care in those hospitals.

Abbreviation and acronyms

DUE: Drug use evaluation, EDL: Essential drug list, WHO: World health organization, HFSUH: Hiwot Fana Specialized Hospital, QH: Quiha Hospital, MH: Mekelle Hospital, INRUD: International Networks for Rational use of medicines.

Ethical Considerations

The study was approved by the institutional review board of Mekelle University (reference number: ERC/224/2019). Based on this a letter of support was written from Tigray regional health bureau. During data collection on patient care indicators, a written consent was obtained from each participant after provision of all the necessary information. In addition, the data collected in the study did not use patient identifiers and were kept strictly confidential and were used only for the purpose of the study. Acknowledgments The authors would wish to thank all the staff members of Mekelle and Quiha hospitals for their sincere cooperation and support.

Competing interests

The authors declare that they have no competing interests. The funder has not any involvement in this study.

Availability of data

The data of this study are available from the corresponding author up on a reasonable request.

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4 registration number of CRPO/CHS/Young/Recurrent/ 008/2011.
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7 **Patient consent for publication**
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9 Not applicable
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12 **Author's contribution**
13

14 SG and AKG designed the study, obtained the fund, supervising data collection, conducted
15 data analysis, wrote the first draft of the manuscript. SG, KG, AKG and HN provide critical
16 comments, revised and finalized the manuscript. All authors read and approved the final
17 manuscript.
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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4 and 5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 and 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5 and 6
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	--
		(d) If applicable, describe analytical methods taking account of sampling strategy	--
		(e) Describe any sensitivity analyses	--
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	--
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	---
Outcome data	15*	Report numbers of outcome events or summary measures	7-11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	---
		(b) Report category boundaries when continuous variables were categorized	---
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	----
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	---
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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3 Assessment of drug use pattern using WHO core drug use indicators in selected general
4 hospitals: a cross-sectional study in Tigray region, Ethiopia

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15 16 Abstract

17
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19 **Objective:** Inappropriate use of medicine is a global challenge with greater impact in
20 developing countries. Assessment of drug use pattern is used to identify gaps in medicine
21 utilization to implement strategies for promoting rational drug use. This study was aimed to
22 assess drug use pattern using the World Health Organization (WHO) drug use indicators in
23 selected general hospitals in Tigray region, Ethiopia.

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28 **Design:** A cross-sectional study was conducted using WHO drug use indicators in two public
29 hospitals located in Tigray.

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33 **Setting:** Prescriptions recorded from January 1, 2017 to June 1, 2019 were randomly selected
34 and participants who visited the public hospitals from March 1, 2019 to August 30, 2019 and
35 hospital pharmacies were interviewed.

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39 **Participants:** 100 patients who visited both outpatient clinics and hospital pharmacy
40 departments of the public hospitals.

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53 **Results:** The average number of medicines per prescription was 1.69 (± 0.81). Prescriptions
44 containing antibiotics and injectables were 58.2% and 15.9% respectively. The percentage of
45 medicines prescribed with a generic name from essential medicines list of Ethiopia were 97.5%
46 (974) and 88.1% (970) in Mekelle and Quiha hospital, respectively. The patients spent an
47 average of 6.56 (± 3.48) minutes with their General Practitioners, whilst only 22.79 (± 21.7)
48 seconds with their pharmacists. Of the patients interviewed, 56.9% knew their dosing regimen
49 and 32.7% of them had their medication labelled.

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60 **Conclusion:** The finding of the present study revealed deviation of drug use pattern from the
55 WHO optimal levels suggesting the hospitals had limitations in appropriate utilization of
56 medicines. Understanding the factors that attributed for the observed gaps and implementing

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3 corrective measures are required to conform with the recommended standards of appropriate
4 drug utilization.
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7 Keywords: Drug use evaluation, Prescribing Indicator, Patient Care Indicator, Facility
8 Indicator
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10 11 **Strengths and limitations of study** 12

- 13
14 • The study utilized all three of the WHO core drug use indicators to assess quality of
15 patient care in hospital setting.
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- 17 • An evidence about rational drug use has been provided in an area rarely assessed.
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- 19 • The study did not try to identify the factors that contributed for the observed gaps
20 making it difficult to propose improvement strategies.
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- 22 • As diagnosis was missing in considerable number of prescriptions, we did not confirm
23 that the drugs were prescribed for right diagnoses.
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Introduction

The rational use of drugs depends on rational prescribing, correct dispensing and adherence to treatment by patients¹. According to the World Health Organization (WHO), a medicine is used rationally if patients received appropriate medicines, in doses that meet their individual requirements, for an adequate period of time and with an affordable cost². The concept of rational drug use can be summarized as the right medicine at the right dose by the right route at the right time for the right patient ('five rights')³. Conversely, irrational use of medicines is termed to have occurred when one or more of the above-mentioned conditions are not met². Irrational use of medicine is a global challenge with the highest prevalence in developing countries. Multiple stakeholders including patients, prescribers, workplace, supply system may attribute for irrational drug use⁴ due to many reasons such as limited knowledge about medicines, unethical medicine promotions and improper prescribing habits of clinicians^{5 6}.

WHO drug use indicators are used to evaluate rational drug use at all levels in the chain of medicine utilization (facility, clinician, pharmacist, and patient) using highly standardized indicators developed by WHO Action Program on Essential Drugs and International Network for Rational Use of Drugs (INRUD) to be used for drug use evaluations without further national validation^{7 8}. Prescribing indicators include average number of medicines prescribed per encounter, percentage of those prescribed by generic name and those from national essential medicines list, percentage of encounters with antibiotics and those with injections prescribed. Patient care indicators are used to evaluate the interaction between the patients with their clinicians and pharmacists and includes average consultation and dispensing times, percentage of medicines dispensed and those adequately labelled, as well as patients' knowledge of correct dosage. The availability of copy of essential medicine list and key medicines are assessed using facility indicators⁹.

Ethiopia has introduced a national drug policy in 1993 with the aim of meeting the demand for essential medicines together with appropriate use, making them affordable to the public as well as ensuring their safety, efficacy, and quality. The policy also encourages domestic manufacturing, enhancing manpower training and research and development of medicines as well as devising ways to integrate traditional medicines into conventional medicine as objectives¹⁰. Despite these policy directions' studies conducted so far reported gaps in rational medicine use^{11 12}. Considering the very large population size of Ethiopia and the diversity of geographic areas, there are very few studies on medicine use conducted so far. Therefore, this

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3 study was conducted to evaluate drug use and contribute to addressing the information gap in
4 drug use pattern in Ethiopia specifically Tigray region.
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7 **Methods and Materials**

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9 **Study setting and period**

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11 The study was conducted in Mekelle and Quiha general hospitals between March 1, 2019 and
12 August 30, 2019. Both hospitals are located in Mekelle, the capital city of Tigray regional state,
13 Ethiopia.
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17 **Study design and population**

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19 All prescriptions recorded from January 1, 2017 to June 1, 2019 were considered. Of which,
20 randomly selected prescriptions were retrospectively assessed using WHO prescribing
21 indicators during the study period [March 1, 2019 and August 30, 2019]. All patients who
22 visited outpatient departments of Mekelle and Quiha hospitals during the study period were
23 used as a target population. Of note, patients aged less 18 years or not willing to participant in
24 the study were excluded.
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31 **Sampling technique and procedure**

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33 WHO recommends assessments of at least 600 prescriptions and 100 patients per each hospital
34 for drug use evaluation. Accordingly, 600 randomly selected prescriptions recorded from
35 January 1, 2017 to June 1, 2019 from each hospital were included. Twenty key drugs were also
36 selected from each hospital as per WHO recommendation which is a minimum of 15 essential
37 drugs for each health facility⁹.
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43 **Data collection instruments and process**

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45 Three well-trained pharmacists were recruited and deployed to assess the prescriptions
46 identified using prescription registration books, interview patients and evaluate availability of
47 copy of essential medicine list and key medicines in the hospitals. Data on quality of
48 prescribing was collected by using WHO's prescribing indicators. In assessing patient care
49 indicators, the average number of medicines prescribed per encounter, the percentage of
50 medicines prescribed with generic names and those prescribed from essential medicine list, the
51 percentage of prescription encounters which ended up with antibiotics and those with injections
52 prescribed were collected. However, immunizations of children were not considered as
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3 injections. In measuring the proportion of medicines prescribed with generic names, the
4 essential medicine list of Ethiopia was used as source for generic names¹³.
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7 For assessment of patient care indicators, consultation time and dispensing time was obtained
8 by recording the time that the patients spent with their physicians and pharmacists respectively.
9 The knowledge of the patients on their dosage regimen were assessed by asking the patients to
10 explain whether they knew about the medicine dispensed for them. Availability of formulary,
11 essential drugs, standard treatment guidelines, and key drugs at the time of the visit were
12 assessed to confirm whether the hospitals comply with WHO standards.
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17 18 **Operational definitions**

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20 Drug use evaluation is a systematic approach that assesses the appropriateness, safety, and
21 effectiveness of a medications to improve patient care.
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25 **Percentage of drugs prescribed by generic name:** It measures the tendency to prescribe by
26 generic name.
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29 **Percentage of drugs prescribed from list of essential drugs:** It measures the degree to which
30 practices conform to a national drug policy.
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33 **Average number of drugs per encounter:** Average number of drugs per encounter measures
34 the degree of poly pharmacy.
35

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37 **Average consultation time:** The average time that physicians spend with patients. It doesn't
38 include waiting time.
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41 **Average dispensing time:** The average time that pharmacists spend with patient while
42 dispensing the medications.
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45 **Data Analysis Procedure**

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47 The data collected were entered and analyzed using Statistical Packages for Social Sciences
48 (SPSS) version 20. The data on prescribing indicators as well as patient care indicators were
49 described using frequency, percentage, mean and standard deviation (SD).
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52 **Patient and Public Involvement**

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54 Patient and/or the public were not directly involved in this study.
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Results

Prescribing indicators

A total of 1200 prescriptions, 600 from each hospital were evaluated using WHO prescribing indicators. On average, 1.69 (± 0.81) drugs were prescribed and 44.7% of the prescriptions contain one or two drugs (**Table 1**).

Table 1: Number of drugs per prescribing encounter in the selected general hospitals

Number of drugs	Quiha hospital n (%)	Mekelle hospital n (%)	Overall result N (%)	WHO standard ¹⁴
One	306 (51)	286 (47.7)	592 (49.7)	
Two	206 (34.3)	214 (35.7)	420 (35)	
Three	72 (12)	82 (13.7)	154 (12.9)	
Four	15 (2.5)	17 (2.8)	32 (23.5)	
Five	1 (0.2)	1 (0.2)	2 (0.2)	
Average	1.67 (± 0.8)	1.72 (± 0.82)	1.69 (± 0.81)	≤ 2 (1.6-1.8)

A total of 2028 drugs were prescribed of which 1944 (92.8%) were prescribed in generic name. More than fifty percent (58.2%) of the prescriptions contained antibiotics and 191 (15.9%) include at least one injectable medication (**Table 2**). Amoxicillin was the most frequently prescribed antibiotic in both hospitals (**Table 3**).

Table 2: Percentages of encounters with generic drugs, antibiotics, and injections in the selected general hospitals

Prescribing indicators		Quiha hospital	Mekelle hospital	Overall result (N)	WHO standard ¹⁴
Generic prescription	Drugs prescribed, n	999	1029	2028	
	Drugs prescribed in generic name, n (%)	974 (97.5)	970 (94.3)	1944 (95.6)	
Antibiotics	Prescriptions with antibiotics, n (%)	392 (65.3)	306 (51)	698 (58.2)	< 30% (20–26.8)
Injections	Prescriptions with injections, n (%)	56 (9.3)	135 (22.5)	191(15.9)	13.4–21.1%
Drugs from essential drug list, n (%)		974 (97.5)	930 (90.4)	1904 (93.9)	100%

Table 3: Antimicrobial/Antibiotics prescribed in the selected general hospitals

Class of Antimicrobial agent	Frequency, n		Overall
	Quiha hospital	Mekelle hospital	
Amoxicillin	160	76	236
Ciprofloxacin	56	44	100
Ceftriaxone	33	57	90
Metronidazole	42	40	82
Antibacterial agents Cephalexin	20	35	55
Amoxicillin /Clavulanic acid	15	28	43
Azithromycin	19	16	35
Cloxacillin	21	11	32
Norfloxacin	17	11	28
Sulfamethoxazole/Trimethoprim	13	11	24
Doxycycline	13	7	20
Ampicillin	1	9	10
Clarithromycin	8	1	9
Erythromycin	2	2	4
Gentamycin	1	2	3
Ceftazidime	-	2	2
Crystalline Penicillin	-	1	1

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2					
3	Antiprotozoal/anthelmintics	Tinidazole	14	17	31
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5		Albendazole	16	7	23
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7		Mebendazole	11	5	17
8					
9		Coarthem	2	-	2
10					
11		Praziquantel	1	-	1
12	Antifungal	Ketoconazole	4	-	4
13					
14		Clotrimazole vaginal supp	3	-	3
15					
16		Fluconazole	1	-	1
17					
18	Antiviral	Acyclovir	2	-	2
19					

20 Amoxicillin or Amoxicillin / Clavulanic acid, and Ceftriaxone were commonly prescribed antibiotics

Patient care indicators

On average each patient spent approximately 7 minutes with his/her General practitioner and 22 seconds with his/her pharmacist. 81.2% of the prescribed drugs were dispensed. Of which, 32.7% of them were adequately labelled. 56.9% of the patients knew about their dosage regimen of their medications (**Table 4**).

Table 4: Assessment of patient care using WHO patient care indicators in selected general hospitals

Patient care indicators	Quiha hospital	Mekelle hospital	Overall	WHO standard
Average consultation time (Minute)	3.66±2.19	9.46±4.77	6.56±3.48	10 min
Average dispensing time (Sec)	21.53±19.89	24.04±23.5	22.79±21.7	>180 seconds
Total number of drugs prescribed	189	171	360	
Total number of drugs dispensed	170	124	294	
Percentage of drugs actually dispensed	89.9	72.5	81.2	100%
Number of drugs adequately labelled	29	50	79	
Percentage of drugs adequately labelled	15.4	50	32.7	
Knows dosage	25(25%)	48 (88.8%)	56.9	

Health facility indicators

Both Quiha and Mekelle hospitals had their own formulary, essential drug list and standard treatment guideline. From the list of key drugs of the hospitals, on average 77.5% of them were available in stock (**Table 5**).

Table 5: Availability of key drugs in selected general hospitals

List of key drugs	Quiha hospital	Mekelle hospital
Amoxicillin/clavulanic acid	✓	X
Ciprofloxacin tablet	✓	X
Cloxacillin capsule	✓	X
Azithromycin	✓	X
Diclofenac injection	✓	✓
Diclofenac tablet	✓	✓
Tramadol	X	✓
Metronidazole	✓	✓
Insulin	✓	✓
Nifedipine	X	✓
Lasix	X	✓
Spironolactone	X	✓
Ceftriaxone	✓	X
Vancomycin	✓	✓
Metformin	✓	✓
Enalapril	✓	✓
Cephalexin	✓	✓
Ferrous sulphate	✓	✓
Paracetamol syrup	✓	X
Amlodipine	✓	X

Discussion

In this study, the average number of drugs per prescription was within the WHO acceptable standard. The finding was comparable with studies done in different parts of Ethiopia including Jimma (1.59)¹⁵, Hawassa University Teaching Referral (1.9)¹¹ and Bahir Dar hospital (1.8)¹². However, studies in Debre Tabor (2.2)¹², Felege Hiwot referral hospital (2.49)¹⁶ and Karamara public general hospital in Ethiopia (2.46)¹⁷ reported higher average number of drugs per prescription. Such discrepancy may be attributable to difference in the level of awareness among clinicians working in different part of the country and lack of harmonized national prescribing guidelines.

In terms of percentage of medicines prescribed by generic name, our finding is lower than the WHO's recommended standard value. Similar results were reported in Hawassa University hospital (98.7%)¹¹, Felege Hiwot specialized University hospital (97.4 %)¹⁶ and selected health centres in eastern Ethiopia (97 %)¹⁸. This may be attributable to increasing promotion of brand drugs names influencing clinicians to prescribe drugs in their brand names. Of note, Workneh *et al* (2016) has shown the prescribing decision of clinicians working in Mekelle were influenced by promotion of medical representatives¹⁹. This suggests that there is a gap in ensuring patients to get cost-effective medicines on the side of prescribers and the health institution, which in turn reduce health seeking behaviour of the community²⁰.

The percentage of encounters with antibiotics, which is 58.2% in the present study is comparable with study conducted in public hospitals in eastern Ethiopia (57.9%)¹⁷, and Hawassa teaching referral hospital (58.1%)¹¹. As high as 85.5% were also reported in selected health centres in eastern Ethiopia¹⁸. However, our finding is higher than WHO recommended standard (20%-26.8%). This finding should be interpreted cautiously as high prevalence of infectious disease in developing countries may partly contributed for such high antibiotic prescribing. However, overprescribing of antibiotics is problematic that need to be carefully monitored as it is associated to antimicrobial resistance which is threat of global health²¹. The percentage of prescriptions encounters with injections were within WHO standard level.

WHO recommends health care professionals to adhere to national essential medicine for drug prescribing. To this end, a deficiency was noted in terms of prescribing according to essential medicine list of Ethiopia compared to the WHO standard of a 100%⁸ and to that of the national assessment results of 2003 (99%)²². This may be attributable to patient preference, clinician decision and availability of the medications.

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3 In this study the average consultation time that the patients spent with clinicians was
4 approximately 7 minutes which is higher compared with studies conducted in public hospitals
5 in eastern Ethiopia (4.6 minutes)¹⁷. The duration, however, doesn't seem to be sufficient for to
6 make physical examination and select the best available treatment choices. High patient load
7 could have contributed for such below the optimal duration of consultation time. The average
8 dispensing time recorded in the present study was approximately 23 seconds. This is
9 significantly lower than the WHO recommendation which is 180 seconds⁸. The lower the
10 dispensing time the poorer would be the understanding of the patients about their medications
11 which this may lead to frequent encounter of drug therapy problems. The percentage of drugs
12 actually dispensed out of the total drugs prescribed to the patients stood at 80 % compared to
13 the recommended 100%⁶. Frequent stock out of medicines may account for this finding.
14 Regarding the adequacy of labelling of medicines dispensed, only slightly over one-third of
15 medicines were appropriately labelled which is far from the recommended level, 100%⁸. High
16 patient load encountered at outpatient pharmacy department and negligence of the pharmacists
17 together with poor concern and follow up from the hospital side could be implicated for such
18 low level of performance in this indicator. Of note, only about half of the patients knew the
19 dosage schedules of their medicines prescribed to them, which is far below the expected level,
20 100%.

21
22 Both Quiha and Mekelle hospital had their own essential drug list and standard treatment
23 guideline. Only 7.5% of key drugs were in stock and this is low with 100% of the WHO
24 recommendation. Absence of key drugs may impair patient care and compromise patient
25 quality of life.

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Conclusion

The findings of the present study showed prescribing practices of antibiotics, prescribing from essential drug list and injections were not within the acceptable WHO recommendations. Overuse of antibiotics facilitate the emergence of antimicrobial resistance which is threat for global health. There was a little deviation in terms of generic prescribing, whereas the average number of drugs per encounter was within the acceptable standard. Poor generic prescribing coupled with shorter consultation and dispensing time may lead to frequent encounters of drug therapy problems. Future studies should investigate underlying factors that contributed for the observed gaps to improve patient care in those hospitals.

Abbreviation and acronyms

EDL: Essential drug list, WHO: World health organization, , QH: Quiha Hospital, MH: Mekelle Hospital, INRUD: International Networks for Rational use of medicines.

Ethical Considerations

The study was approved by the institutional review board of Mekelle University (reference number: ERC/224/2019). Based on this a letter of support was written from Tigray regional health bureau. During data collection on patient care indicators, a written consent was obtained from each participant after provision of all the necessary information. In addition, the data collected in the study did not use patient identifiers and were kept strictly confidential and were only used for the purpose of the study.

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Competing interests

The authors declare that they have no competing interests. The funder has not any involvement in this study.

Availability of data

The data of this study are available from the corresponding author up on a reasonable request.

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Patient consent for publication

Not applicable

Author's contribution

SG and AKG designed the study, obtained the fund, supervising data collection, conducted data analysis, wrote the first draft of the manuscript. SG, KG, AKG and HN provide critical comments, revised and finalized the manuscript. All authors read and approved the final manuscript.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4 and 5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 and 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5 and 6
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	--
		(d) If applicable, describe analytical methods taking account of sampling strategy	--
		(e) Describe any sensitivity analyses	--
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	--
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	---
Outcome data	15*	Report numbers of outcome events or summary measures	7-11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	---
		(b) Report category boundaries when continuous variables were categorized	---
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	----
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	---
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.